



# UNITED STATES PATENT AND TRADEMARK OFFICE

WY  
UNITED STATES DEPARTMENT OF COMMERCE  
United States Patent and Trademark Office  
Address: COMMISSIONER FOR PATENTS  
P.O. Box 1450  
Alexandria, Virginia 22313-1450  
www.uspto.gov

| APPLICATION NO.   | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|-------------|----------------------|---------------------|------------------|
| 10/706,892  | 11/13/2003  | Pei-Yong Shi         | 454311-2231.1       | 1951             |
| 20999   | 7590        | 06/02/2006           |                     | EXAMINER         |
| FROMMER LAWRENCE & HAUG<br>745 FIFTH AVENUE- 10TH FL.<br>NEW YORK, NY 10151 |             |                      | SALVOZA, M FRANCO G |                  |
|   |             |                      | ART UNIT            | PAPER NUMBER     |
|   |             |                      | 1648                |                  |

DATE MAILED: 06/02/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

| <b>Office Action Summary</b> | Application No.   | Applicant(s) |
|------------------------------|-------------------|--------------|
|                              | 10/706,892        | SHI ET AL.   |
|                              | Examiner          | Art Unit     |
|                              | M. Franco Salvoza | 1648         |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

1)  Responsive to communication(s) filed on 02/28/06.

2a)  This action is **FINAL**.                            2b)  This action is non-final.

3)  Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

4)  Claim(s) 1-94 is/are pending in the application.  
4a) Of the above claim(s) 2,18,19,22-27,33-44,70-92 and 94 is/are withdrawn from consideration.  
5)  Claim(s) \_\_\_\_\_ is/are allowed.  
6)  Claim(s) 1,32,45-69 and 93 is/are rejected.  
7)  Claim(s) 3-17, 20, 21, 28-31 is/are objected to.  
8)  Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

9)  The specification is objected to by the Examiner.

10)  The drawing(s) filed on 11/13/03 is/are: a)  accepted or b)  objected to by the Examiner.

    Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

    Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)  The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)  Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a)  All    b)  Some \* c)  None of:  
1.  Certified copies of the priority documents have been received.  
2.  Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
3.  Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1)  Notice of References Cited (PTO-892)  
2)  Notice of Draftsperson's Patent Drawing Review (PTO-948)  
3)  Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date 03/07/05.

4)  Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_ .  
5)  Notice of Informal Patent Application (PTO-152)  
6)  Other: \_\_\_\_ .

## **DETAILED ACTION**

### ***Election/Restrictions***

Applicant's election with traverse of Group I, claims 1, 3-17, 20, 21, 28-32, 45-69, 93 in the reply filed on February 28, 2006 is acknowledged.

The traversal is on the ground(s) that the inventions I, II, V, VII, VIII, IX, X share the same classification; the inventions depend from or recite limitations of Group I; no serious burden would be imposed on the examiner to search I, II, III, V, VI, VII, VIII, IX, X; such searches would be coextensive; the inventions recite a web of knowledge and continuity of effort; if the members of a Markush group are sufficiently close in number, closely related, they must be examined if a search can be made without serious burden.

Applicant's arguments are considered but found unpersuasive.

While the inventions and methods may be related, the appropriate standard to apply regarding restriction requirement is not whether or not the inventions are closely related or belong in the same class and subclass, rather whether the inventions are independent and distinct over one another. The rationale supporting the restriction to independent and distinct inventions is made of record in the Restriction Requirement.

Further, the inventions recite recognized divergent subject matter as recited in the Restriction requirement, imposing a serious burden as searches required for any one of the groups or species would be independent of the others.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1, 3-17, 20, 21, 28-32, 45-69, 93 are pending and under consideration.

***Claim Objections***

Claims 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 20, 21, 28, 29, 30, 31 are objected to under 37 CFR 1.75(c) as being in improper form because they recite multiply dependent claims or depend from such claims, i.e.: "the system according to claims 1 and 2," etc. See MPEP § 608.01(n).

Accordingly, claims 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 20, 21, 28, 29, 30, 31 have not been further treated on the merits.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Chambers et al. (1999).

Claim 1 recites a reverse genetics system for screening and identifying antiflaviviral compounds.

Chambers et al. teaches the use of reverse genetics systems to create chimeric flaviviruses that can induce neutralizing antibodies and be used for screening and identifying antiflaviviral compounds (p. 3095).

Claim 1 is also rejected under 35 U.S.C. 102(b) as being anticipated by Lai et al. (1998).

See the recitation of claim 1 above.

Lai et al. teaches reverse genetics systems and attenuated backbones to construct chimeric flaviviruses for DEN-4 that can be used in screening and identifying antiflaviviral compounds (p. 173).

Claim 1 is also rejected under 35 U.S.C. 102(b) as being anticipated by Yamshchikov et al. (2001).

See the recitation of claim 1 above.

Yamshchikov et al. teaches reverse genetics systems and a replicon of WNV that can be used in screening and identifying antiflaviviral compounds (p. 294).

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1, 32, 59, 61, 62, 66 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shi et al. (“Infectious cDNA Clone of the Epidemic West Nile Virus from New York City”; (2002)) in view of Hicks.

Claim 1 recites a reverse genetics system for screening and identifying antiflaviviral compounds.

Claim 32 recites recombinant plasmid containing a cDNA sequence corresponding to WNV lineage 1, wherein said recombinant plasmid further comprises a promoter sequence adapted to control cDNA transcription and at least one nucleotide sequence encoding a reporter, wherein said reporter indicates the level of transcription of said cDNA sequence corresponding to WNV lineage 1.

Claims 59, 61, 62, 66 recite a DNA molecule comprising a DNA sequence encoding a full-length and fully-infectious mRNA of a lineage I WNV genome, said DNA sequence having a 5' and a 3' end, said DNA molecule adapted to report the transcription of said DNA sequence, said DNA molecule comprising: (a) a promoter at said 5' end of said DNA sequence; (b) a first nucleotide sequence encoding a first reporter gene at said 3' end of the DNA sequence; wherein said promoter is adapted to control the transcription of said DNA sequence and said reporter gene; wherein said reporter is selected from the group consisting of green fluorescent protein; wherein said promoter is selected from T7.

Shi et al. teaches a plasmid with a cDNA sequence corresponding to West Nile virus lineage I comprising a T7 promoter sequence (p. 5848) and IFA to detect expression. Shi et al. also teaches a DNA sequence encoding a full length and fully infectious mRNA of WNV lineage I, having a 5' and 3' end with a promoter.

Shi et al. does not teach the use of a reporter gene such as GFP.

Hicks teaches the use of GFP to monitor nucleic acid transcription of viral genomes (p. 297).

One of ordinary skill in the art at the time the invention was made would have been motivated to combine the DNA sequence of Shi et al. and the GFP of Hicks because Hicks

et al. teaches that GFP permits detection of viral expression without the need to wait for overt cytopathic effect (CPE) or for fixing cells.

One of ordinary skill in the art at time the invention was made would have had a reasonable expectation of success for using the DNA sequence of Shi et al. and the GFP of Hicks et al. because Shi et al. and Hicks both teach nucleic acid transcription.

Therefore, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, absent unexpected results to the contrary.

Claims 67, 68, 69 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shi et al. and Hicks in view of Khromykh et al.

Claims 67-69 recite the DNA molecule according to claim 59, wherein said DNA molecule comprises a second nucleotide sequence encoding a second reporter, wherein the transcription of said second nucleotide sequence encoding the second reporter is under control of said promoter; wherein the second reporter is selected from the group consisting of green fluorescent protein; wherein the first and second nucleotide sequences encoding said first and second reporters are optionally preceded by an internal ribosome entry site (IRES), wherein said IRES facilitates translation of said first and second reporters.

See the teachings of Shi et al. and Hicks above.

Shi et al. and Hicks do not teach the use of a second reporter gene wherein the first and second reporter gene are preceded by an IRES.

Khromykh et al. teaches the use of a two reporters (here, CAT and Neomycin gene) controlled by an IRES to monitor transcription in host cells as well as to enable selection of host cells expressing desired proteins (p. 1497).

One of ordinary skill in the art at the time the invention was made would have been motivated to combine the DNA sequence and GFP of Shi et al. and Hicks and the second reporter wherein both reporters are optionally preceded by an IRES of Khromykh et al. because Khromykh et al. teaches the addition of a second reporter to enable selection of host cells containing desired proteins.

One of ordinary skill in the art at time the invention was made would have had a reasonable expectation of success for using the DNA sequence and GFP of Shi et al. and Hicks et al. and the second reporter and IRES of Khromykh et al. because Shi et al. and Hicks and Khromykh et al. both teach nucleic acid transcription.

Therefore, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, absent unexpected results to the contrary.

Claims 1, 32, 45, 50, 51, 54, 55, 57, 93 are rejected under 35 U.S.C. 103(a) as being unpatentable over Khromykh et al. in view of Chambers et al. supported by Barrett.

See the recitations of claims 1, 32 above.

Claim 45 recites a DNA molecule comprising a DNA sequence encoding a mRNA of a lineage I WNV genome, said DNA sequence having a 5' and a 3' end, said DNA molecule adapted to report the transcription of said DNA sequence, said DNA molecule comprising:

(a) a deletion in said DNA sequence corresponding to one or more structural genes of said lineage 1 WNV genome', (b) a promoter at said 5' end of said DNA sequence; (c) a nucleotide sequence encoding a reporter at said 3' end of the DNA sequence; wherein said promoter is operably linked and adapted to control the transcription of said DNA sequence and said nucleotide sequence encoding said reporter.

Claim 50, 51, 54 recite the DNA molecule according to claim 45, wherein said one or more structural genes is selected from the envelope; wherein said deletion is in the envelope, of said lineage I WNV genome; wherein said promoter is selected from the group consisting of SP6, T7, and T3.

Claims 55, 57 recite the DNA molecule according to claim 45, wherein said DNA molecule contains a second nucleotide sequence encoding a reporter, wherein transcription of said second nucleotide sequence encoding said second reporter under control of said promoter; wherein the first and second nucleotide sequences encoding first and second reporters are optionally preceded by an internal ribosome entry site (IRES), wherein said IRES facilitates translation of said first and second reporters.

Claim 93 recites a cell line comprising the DNA molecule according to claim 45.

Khromykh et al. teaches replicons of the Kunjin virus (of the flavivirus family) containing large deletions in the structural region encompassing the envelope protein with a CAT reporter gene (p. 1497). Khromykh et al. also teaches the use of a second reporter controlled by an IRES as well as expression in host cells. Khromykh et al. also teaches that Kunjin virus is closely related to West Nile as members of the flavivirus family (p. 1497). Khromykh et al.

teaches the use of the replicons for flaviviral RNA replication as well as a RNA virus expression system.

(Khromykh et al. does not teach the T7 promoter as recited in claim 54. However, the reference teaches the use of subgenomic replicons encoding RNA; the presence of a promoter to induce transcriptions is inherently included in said replicons. Further, one of ordinary skill in the art would know to substitute a T7 promoter for another promoter as they are functional equivalents. See MPEP 2144.06.)

Khromykh et al. does not teach the West Nile Virus lineage I replicon.

Chambers et al. teaches a reverse genetics system using the ChimeriVax platform or nucleic acid backbone wherein the premembrane and envelope protein genes are deleted and substituted with those of other flaviviruses to create cDNAs encoding for chimeric viruses. Chambers et al. teaches that the flaviviruses envelope regions can be deleted and replaced with the envelope regions of other flaviviruses. Barrett in support of Chambers et al. states that the ChimeriVax technology can be applied to West Nile virus (p. 269). (See also Lai et al. (1998) teaching use and substitution of portions of another flavivirus DEN; See also Yamschikov et al. teaching the use of the technology in West Nile virus replicons, lineage II.)

One of ordinary skill in the art at the time the invention was made would have been motivated to combine the flaviviral DNA molecule with a structural protein deletion of Khromykh et al. in West Nile reverse genetics system of Chambers et al. supported by Barrett because Chambers et al. supported by Barrett teaches that the reverse genetics system can be used for other structurally similar flaviviruses such as West Nile since flaviviruses are sufficiently structurally related for purposes of reverse genetics applications.

One of ordinary skill in the art at time the invention was made would have had a reasonable expectation of success for using a flaviviral DNA molecule with a structural protein deletion of Khromykh et al. with the West Nile replicon of Chambers et al. supported by Barrett because both Khromykh et al. and Chambers et al. supported by Barrett teaches the use of reverse genetics systems.

Therefore, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, absent unexpected results to the contrary.

Claims 47, 48, 56, 58 are rejected under 35 U.S.C. 103(a) as being unpatentable over Khromykh et al. and Chambers et al. supported by Barrett in view of Hicks.

Claims 47, 48, 56, 58 recite the DNA molecule according to claims 45 and 55, wherein said reporter is selected from the group consisting of green fluorescent protein. Claim 58 recites the DNA molecule according to claim 45, wherein the DNA sequence is a lineage I WNV replicon and said reporter is GFP.

See the teachings of Khromykh et al. and Chambers et al. supported by Barrett above.

See the teachings of Hicks above.

One of ordinary skill in the art at the time the invention was made would have been motivated to combine the reverse genetics system of Khromykh et al. and Chambers et al. supported by Barrett and the GFP of Hicks because Hicks teaches the GFP reporter gene permits detection of viral expression without the need to wait for overt cytopathic effect (CPE) or for fixing cells.

One of ordinary skill in the art at time the invention was made would have had a

reasonable expectation of success for using the reverse genetics system of Khromykh et al. and Chambers et al. supported by Barrett and the GFP of Hicks because Khromykh et al. and Chambers et al. supported by Barrett and Hicks both teach nucleic acid transcription.

Therefore, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, absent unexpected results to the contrary.

Claims 1, 32, 59 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hurrelbrink et al. in view of Chambers et al. supported by Barrett.

See the recitation to claims 1, 32, 59 above.

Hurrelbrink et al. teaches a plasmid with a genome length cDNA sequence corresponding to Murray Valley virus of the flavivirus family comprising a T7 promoter sequence (p. 3115).

Hurrelbrink does not teach the plasmid with a genome length cDNA sequence corresponding to West Nile virus.

See the teachings of Chambers et al. supported by Barrett above.

One of ordinary skill in the art at the time the invention was made would have been motivated to combine the genome-length flavivirus cDNA sequence of Hurrelbrink et al. and the West Nile reverse genetics system of Chambers et al. supported by Barrett because Chambers et al. supported by Barrett teaches that the reverse genetics system can be used for other structurally similar flaviviruses such as West Nile since flaviviruses are sufficiently structurally related for purposes of reverse genetics applications.

One of ordinary skill in the art at time the invention was made would have had a

reasonable expectation of success for using the genome-length flavivirus cDNA sequence of Hurrelbrink et al. and the West Nile reverse genetics system of Chambers et al. supported by Barrett because Hurrelbrink et al. and Chambers et al. supported by Barrett both teach the use of reverse genetics systems.

Therefore, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, absent unexpected results to the contrary.

Claims 61, 62, 66 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hurrelbrink et al. and Chambers et al. supported by Barrett in view of Hicks.

See the recitations to claims 61, 62, 66 above.

See the teachings of Hurrelbrink et al. and Chambers et al. supported by Barrett above.

Hurrelbrink et al. and Chambers et al. supported by Barrett does not teach the use of a reporter gene such as GFP.

See the teachings of Hicks above.

One of ordinary skill in the art at the time the invention was made would have been motivated to combine the genome cDNA sequence of Hurrelbrink et al. and Chambers et al. supported by Barrett and the GFP of Hicks because Hicks teaches that GFP reporter gene permits detection of viral expression without the need to wait for overt cytopathic effect (CPE) or for fixing cells.

One of ordinary skill in the art at time the invention was made would have had a reasonable expectation of success for using the Hurrelbrink et al. and Chambers et al. supported by Barrett and the GFP of Hicks because Hurrelbrink et al. and Chambers et al. supported

by Barrett and Hicks both teach nucleic acid transcription.

Therefore, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, absent unexpected results to the contrary.

Claims 67, 68, 69 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hurrelbrink et al., Chambers et al. supported by Barrett, Hicks in view of Khromykh et al.

See the recitation to claims 67-69 above.

See the teachings of Hurrelbrink et al., Chambers et al. supported by Barrett, Hicks above.

Hurrelbrink et al., Chambers et al. supported by Barrett, Hicks above do not teach the use of a second reporter gene wherein the first and second reporter gene are preceded by an IRES to facilitate translation.

Khromykh et al. teaches the use of a two reporters (here, CAT and Neomycin gene) controlled by an IRES to monitor transcription in host cells as well as to enable selection of host cells expressing desired proteins (p. 1497).

One of ordinary skill in the art at the time the invention was made would have been motivated to combine the DNA sequence and GFP of Hurrelbrink et al. and Chambers et al. supported by Barrett and Hicks and the second reporter and IRES of Khromykh et al. because Khromykh et al. teaches the addition of a second reporter to enable selection of host cells containing desired proteins.

One of ordinary skill in the art at time the invention was made would have had a

reasonable expectation of success for using the DNA sequence and GFP of Hurrelbrink et al. and Chambers et al. supported by Barrett and Hicks and the the second reporter and IRES of Khromykh et al. because Hurrelbrink et al. and Chambers et al. supported by Barrett and Hicks et al. and Khromykh et al. both teach both teach nucleic acid transcription.

Therefore, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, absent unexpected results to the contrary.

***Allowable Subject Matter***

SEQ ID NO:2 is not taught in the prior art.

***Conclusion***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to M. Franco Salvoza whose telephone number is (571) 272-8410. The examiner can normally be reached on M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on (571) 272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

  
M. Franco Salvoza  
Patent Examiner  
May 23, 2006



**BRUCE R. CAMPELL, PH.D  
SUPERVISORY PATENT EXAMINER  
TECHNOLOGY CENTER 1600**